PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P50572	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US97/20004	International filing date *(day/month/year)* 05 NOVEMBER 1997	Priority date *(day/month/year)* 06 NOVEMBER 1996
International Patent Classification (IPC) or national classification and IPC IPC(6): C12Q 1/68; C07H 21/04; A61K 48/00 and US Cl.: 436/6; 536/23.7; 514/44		
Applicant SMITHKLINE BEECHAM CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04 JUNE 1998	19 FEBRUARY 1999
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JEHANNE SOUAYA Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/20004

I. Basis of the report

1. This report has been drawn on the basis of (*Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments*):

[X] the international application as originally filed.

[X] the description, pages 1-19 , as originally filed.
pages NONE , filed with the demand.
pages NONE , filed with the letter of _____.
pages _____ , filed with the letter of _____.

[X] the claims, Nos. 1-22 , as originally filed.
Nos. NONE , as amended under Article 19.
Nos. NONE , filed with the demand.
Nos. NONE , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

[X] the drawings, sheets/~~fig~~ NONE , as originally filed.
sheets/~~fig~~ NONE , filed with the demand.
sheets/~~fig~~ NONE , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

[X] the description, pages NONE .
[X] the claims, Nos. NONE .
[X] the drawings, sheets/~~fig~~ NONE .

3. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/20004

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-22	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	NONE	YES
	Claims	1-22	NO
Industrial Applicability (IA)	Claims	1-22	YES
	Claims	NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-22 lack an inventive step under PCT Article 33(3) as being obvious over American Cyanamid Company in view of Lennon *et al.* American Cyanamid Company teaches methods of screening for detection of herbicides (abstract) involving formation of microbes containing genes essential for plant growth and screening for compounds that inhibit plant enzymes (page 4 lines 4-5). Additionally American Cyanamid Company teaches that once a herbicidal compound is identified, plant populations may be mutagenized and grown in the presence of the herbicide at a concentration known to be sufficient to inhibit growth of the wild-type and then plants that are able to grow can be selected (page 4, lines 13-17 and lines 36-43). American Cyanamid Company teaches compositions of herbicides (page 18 lines 1-30) and isolated genes and proteins known to be essential to the growth of plants (page 2 line 43, page 18, line 51-58). American Cyanamid Company does not teach the use of a grid immobilized library to perform the screening of mutants. Lennon *et al* teaches methods of screening libraries involving generating a plurality filters that form a grid, each grid containing at a predefined region immobilized cDNA clones (page 314, col. 2 first paragraph, page 315, col. 1 last paragraph and col. 2). Lennon *et al* also teaches the use of a "genomic" cDNA library (page 314, col. 2 last paragraph). Lennon *et al* teaches screening the filters with a labeled hybridization probe to, for example identify cDNAs (equivalent to mRNAs) that are differentially expressed between tissues and/or developmental stages or directly comparing two sets of conditions (Table 1, page 316, col. 2 first full paragraph). Lennon *et al* teaches that the use of arrayed libraries can be used to eliminate the need for multiple rounds of clone purification thereby improving screening methods (page 315 col. 2 last paragraph). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the hybridization based screening method of Lennon *et al* to have screened for mutations in a population grown under defined conditions (e.g. a concentration of herbicide) as taught by American Cyanamid Company to have obtained the invention as a whole. One of ordinary skill in the art at the time the invention was made would have been motivated (Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
to have used the methods of Lennon *et al* for screening to have screened for herbicide resistance as taught by American Cyanamid Company because Lennon *et al* teaches that the use of arrayed libraries can be used to eliminate the need for multiple rounds of clone purification thereby improving screening methods thus addition of the method of screening of Lennon *et al* to the method of American Cyanamid Company would have made the screening method of American Cyanamid Company easier to perform.

Claims 1-22 lack an inventive step under PCT Article 33(3) as being obvious over Nishi *et al* in view of Lennon *et al*. Nishi *et al* teaches an agent (LMB)that induces arrest of the eukaryotic cell cycle (abstract, first paragraph of page 6320). Nishi *et al* teaches screening a genomic library of LMB-resistant mutants to identify the target gene of LMB (abstract and last paragraph page 6320). Nishi *et al* teaches comparison of allelic mutations and wild-type (page 6322, col. 2 first full paragraph). Nishi *et al* teaches the gene and protein sequence of the LMB resistant gene (page 6322, Table II. Nishi *et al* teaches compositions of the agent LMB (Figure 1). Nishi *et al* does not teach the use of a grid immobilized library to perform the screening of mutants. Lennon *et al* teaches methods of screening libraries involving generating a plurality filters that form a grid, each grid containing at a predefined region immobilized cDNA clones (page 314, col. 2 first paragraph, page 315, col. 1 last paragraph and col. 2). Lennon *et al* also teaches the use of a "genomic" cDNA library (page 314, col. 2 last paragraph). Lennon *et al* teaches screening the filters with a labeled hybridization probe to, for example identify cDNAs (equivalent to mRNAs) that are differentially expressed between tissues and/or developmental stages or directly comparing two sets of conditions (Table 1, page 316, col. 2 first full paragraph). Lennon *et al* teaches that the use of arrayed libraries can be used to eliminate the need for multiple rounds of clone purification thereby improving screening methods (page 315 col. 2 last paragraph). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the hybridization based screening method of Lennon *et al* to have screened for LMB mutations in a population grown under defined conditions as taught by Nishi *et al* to have obtained the invention as a whole. One of ordinary skill in the art at the time the invention was made would have been motivated to have used the methods of Lennon *et al* for screening to have screened for LMB target genes as taught by Nishi *et al* because Lennon *et al* teaches that the use of arrayed libraries can be used to eliminate the need for multiple rounds of clone purification thereby improving screening methods thus addition of the method of screening of Lennon *et al* to the method of Nishi *et al* would have made the screening method of Nishi *et al* easier to perform.

Claims 1-22 meet the criteria set out in PCT Article 33(2) and(4), because the prior art does not teach the claimed methods of identifying genes using a plurality of grids comprising an immobilized genomic library nor compositions obtained from this method and such methods and compositions have industrial applicability in the art of gene identification and drug discovery.

———— NEW CITATIONS ————

EP 0 608 722 A1 (AMERICAN CYANAMID COMPANY) 03 August 1994, see pages 3-4 and 18.

NISHI et al. Leptomycin B Targets a Regulatory Cascade of crm1, a Fission Yeast Nuclear Protein, Involved in Control of Higher Order Chromosome Structure and Gene Expression. Journal of Biological Chemistry. 04 March 1994, Vol. 269, No. 9, pages 6320-6324, see entire document.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 10 July 1998 (10.07.98)	
International application No. PCT/US97/20004	**Applicant's or agent's file reference** P50572
International filing date (day/month/year) 05 November 1997 (05.11.97)	**Priority date** (day/month/year) 06 November 1996 (06.11.96)
Applicant MOONEY, Jeffrey, L. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

04 June 1998 (04.06.98)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Jean-Marie McAdams
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

2129020

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/20004

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C12Q 1/68; C07H 21/04; A61K 48/00
US CL : 436/6; 536/23.7; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 436/6; 536/23.7, 24.32; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Searched inventors and keywords: identifying gene growth and library or compar or hybridiz? or nucleic acid or probe array in APS, CAPLUS, MEDLINE, SCISEARCH, BIOSIS WPIDS.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SAPOLSKY et al. Mapping Genomic Library Clones Using Oligonucleotide Arrays. Genomics. May 1996, Vol. 33, No. 3, pages 445-456, see entire document.	1-22
Y	LENNON et al. Hybridization analyses of arrayed cDNA libraries. Trends in Genetics. October 1991, Vol. 7, No. 10, pages 314-317, see entire document.	1-12
Y,P	WO 97/23642 A1 (MICROCIDE PHARMACEUTICALS, INC) 03 July 1997, see abstract and pages 4-7.	1-22
Y,P	WO 97/10365 A1 (AFFYMAX TECHNOLOGIES N.V.) 20 March 1997, see abstract, pages 4-8 and Figure 1.	1-22

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents.	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 12 JANUARY 1998	Date of mailing of the international search report 10 FEB 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer DEBRA SHOEMAKER Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)★